THE EFFECT OF PHENAMINE ON THE MOTOR EXCITATION CAUSED BY BARBITURATES

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Hyperkinesis caused by barbiturates and especially distinctly expressed by small rodents (mice and rats) can be utilized as an object for the study of different substances capable of raising or lowering the excitability of the central nervous system. Hyperkinesis is manifested in 2 forms: 1) in locomotor excitation associated with depression of the cerebral cortex and 2) in the subsequent tremors depending on the exciting action of barbiturates on the brain stem [midbrain (mesencephalon) and even interbrain (diencephalon)]. The latter form of hyperkinesis was formerly called by us "barbiturate hyperkinesis" [2, 3], and we now perfer to call it "brain-stem hyperkinesis."

In the current project we studied the effect of phenamine on both forms of motor excitation caused in mice by hexenal (hexobarbital).

EXPERIMENTAL METHOD

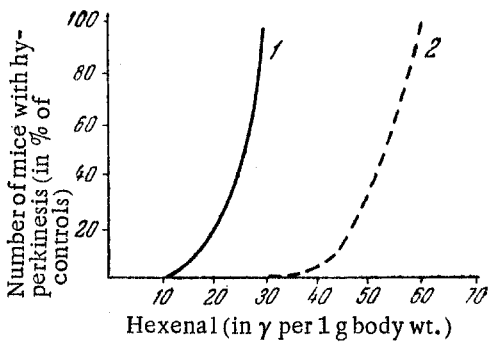
Experiments were carried out on mice of 3 age groups (400 animals): baby mice (weighing 4-5 g), young mice (weighing 10-12 g) and adult mice (weighing 16-18 g). All animals were obtained from one breeding laboratory. The substances studied were administered in aqueous solution subcutaneously in the animal's back. Phenamine was used in doses of 0.1 to 5 γ per 1 g body weight so as not to produce motor excitation in the control animals.

EXPERIMENTAL RESULTS

Preliminary administration of phenamine promoted development of locomotor excitation and brain-stem hyperkinesis from doses of hexenal (15-30 γ per 1 g body weight), which alone, according to our findings, did not produce it (see figure).

During the 6 hours following the administration of phenamine the mice sat quitely in groups within the jars, but when at the end of this interval an optimal dose of hexenal (60-80 γ per g of body weight) was administered the animals entered a state of extreme motor excitation. Especially marked was locomotor excitation and brain-stem hyperkinesis in mice 2-3 weeks of age (weighing 4-5 g). Locomotor excitation was in the form of constant running about (besides, the mice jumped, squeaked, bit one another, etc. Brain-stem hyperkinesis in the animals manifested itself in stronger and more prolonged tremors of the extremities, trunk, head and tail.

In the control group, hexenal (in doses indicated above) produced side reactions in all animals. As is known, phenamine is an antagonist of barbiturates. Therefore, it was not unexpected to observe that side reactions were observed not in all of the experimental animals; brain-stem hyperkinesis manifested itself in them in the form of very quick, small jumps in one place (5 jumps per second, for example) with frequent falling over followed by getting up once more.



Decrease in the dose of hexenal required to produce stem hyperkinesis in adult mice under the effect of phenamine. 1) mice given a preliminary injection of phenamine in the dose of 5 γ per 1 g of body weight (25 animals); 2) mice given hexenal only (25 animals).

It must be pointed out that in mice of different batches (from different breeding laboratories) phenamine may fail to produce motor excitation, even when administered in relatively large doses. Low sensitivity in mice was observed in their experiments in our department by Ts'in Wo-i/ Ch'ih chih-ts'ien', they observed a sharp increase in locomotor excitation in mice caused by hexenal (60-80 γ per 1 g body weight) following preliminary administration of phenamine in doses as small as 15-20 γ per 1 g body weight).

The phenomenon of brain-stem hyperkinesis demonstrates clearly the antagonism between phenamine and morphine (or proserine). Administration of morphine in doses of 0.5-2 γ per 1 g body weight (or proserine in doses of 0.01-0.1 γ per 1 g body weight) prevents the development of brain-stem hyperkinesis from hexenal in doses already indicated [1, 2]. But if morphine (or proserine) is administered together with phenamine, the latter prevents the depressing effect of morphine (or proserine) and hyperkinesis develops as usual.

According to the literature, the exciting effect of phenamine spreads to the cortex and brain stem. Inasmuch as phenamine does not produce hyperkinesis originating in the brain stem, it must be concluded that it increases the barbiturate brain-stem hyperkinesis. Earlier we demonstrated that under the influence of small doses of paraldehyde or ether which do not cause motor excitation in mice, brain-stem hyperkinesis is produced by hexenal in doses which are ineffective in control animals. This effect was explained by us as due to disinhibition of motor centers of the brain stem [4]. Increase in motor excitation, produced by hexenal, by the preliminary adminstration of phenamine is sharper than that due to the moderate narcotic action of ether and has a different localization.

SUMMARY

The following was established in experiments on mice. Preliminary administration of phenamine (0.1-5.0 γ per kg of body weight) considerably intensifies the locomotor excitation and the brain stem hyperkinesis caused by hexenal (60-80 γ/g). Hyperkinesis is especially intensified in 2-3-week-old mice weighing 4 to 5 gms. After a preliminary administration of phenamine the locomotor excitation and the hyperkinesis are caused by doses of hexenal (10-30 γ per gm. of weight) which do not cause these phenomena in the control animals. Locomotor excitation caused by hexenal is intensified by the preliminary moderate administration of phenamine much more than by preliminary narcotic action of ether or paraldehyde. Phenamine removes morphine and proserine depression of barbiturate brain-stem hyperkinesis in mice. The effect of phenamine is antagonistic to that of morphine and proserine.

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*Original Russian pagination. See C. B. Translation.